

Statistical Analysis Plan

TRIAL FULL TITLE	How Point-of-Care Ultrasound Affects the Diagnostic Process in General Practice. A Prospective Follow-up Study.
Danish working title	GULD-forskningsprojektet: God ultralyds diagnostik i almen praksis.
Clinical Trials reg.number	NCT03375333
SAP VERSION	2.0 2019-02-12
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2 Abbreviations and Definitions

GP	General practitioner
US	ultrasound
POC-US	Point-of-care ultrasound
RUGP-Aalborg	Research unit for General Practice in Aalborg, Department of clinical medicine Aalborg University, Denmark
ICPC2	International Classification of Primary Care – 2nd Edition Wonca International Classification Committee
ID	Identification
PatientID	Unique identification number on patients used in this study
Q1-19.1	Collected variables in the questionnaire
T1	Collected variable= time registration of finished Question 11
T2	Collected variable = time registration of start Q12
T3	Calculated variable = time in seconds between T1 and T2
FUS	Calculated variable, frequency of POC-US for each GP
NDB	Calculated variable, number of tentative diagnoses before POC-US
NDA	Calculated variable, number of tentative diagnoses after POC-US
CMD	Calculated variable, change in the main tentative diagnosis
CND	Calculated variable, change in the total number of tentative diagnoses
CSD	Calculated variable, change from symptom to disease diagnosis
BQ	Background questions for the participating GPs
OSAUS	Objective structured assessment of ultrasound skills

3 Introduction

3.1 General introduction

Point-of-care ultrasound (POC-US) is increasingly used moving into general practice as an extension of the physical examination of patients. Potentially there are great advantages of using POC-US: It may lead to more correct diagnoses, and change the plan or treatment of the patients in general practice. However, an increased use of US imaging may lead to overdiagnosis, spurious findings, incidental findings or diagnosing of clinically unimportant conditions.

Future GPs will be familiar with the technology as POC-US is part of the medical education at the university and the postgraduate specialization to become a general practitioner. To gain the benefits and avoid unnecessary harm by the utilization of POC-US in general practice it is crucial that the use of POC-US in a general practice setting is properly evaluated.

3.2 Purpose of the analyses

The aim of this study is to describe: How general practitioners use POC-US in their daily practice, how POC-US influences the diagnostic process, and how POC-US affects the treatment of the patients.

4 Study Objectives and Endpoints

4.1 Study Objectives

4.1.1 The Use of POC-US

Explored through *indication, frequency, time consumption, modification, and findings* in order to describe:

- Which organs the GPs scan, when using POC-US?
- Which tentative diagnoses entail the use of POC-US?
- If GPs intend to rule-in/rule-out or explore, when using POC-US?
- How often the GPs use POC-US?
- How often are the GPs able to produce POC-US pictures of relevant structures?
- How much time POC-US adds to the consultation?
- How often a difference in what the GP intends to scan and what POC-US is actually used for occurs (modification of the performed POC-US)?
- How often POC-US leads to a specific finding?

4.1.2 Influence on the diagnostic process

The influences of the diagnostic process will be explored through change in the tentative diagnosis and change in the GP's confidence in the tentative diagnosis. We aim to describe:

- If POC-US changes the patient's tentative diagnosis
- If POC-US increases the GP's confidence in the tentative diagnosis
- The relationship between the GP's expression of confidence and change in the number of tentative diagnoses
- The relationship between change from symptom diagnoses to disease diagnoses and the GP's expression of confidence in the tentative diagnosis
- The relationship between specific organs scanned and the GP's expression of confidence in the tentative diagnosis

4.1.3 Effects on the treatment of patients

The effects on the treatment of patients will be explored through changes in the plan or treatment for the patient. We aim to describe:

- If POC-US changes the GP's plan for the patient
- If POC-US changes the treatment for the patient
- The relationship between findings and change in the plan or treatment for the patient.

5 Endpoints

5.1 How general practitioners use POC-US in their daily practice:

The use of POC-US will be examined through the domains *indication, frequency, time consumption, modification, and findings*.

5.1.1 Indication:

The GP's indication for using POC-US will be described through the frequencies of the GP's intention to *rule-in/ rule-out, or explore* when using POC-US (Q6).

The indication will also be described through frequencies of the tentative diagnoses (Q8 and Q9.1)) that entail the use of POC-US.

5.1.2 Frequency:

How frequently POC-US is used will be described as the percentage of the GP's consultations, where POC-US is used in the study period (number of included and excluded patients out of the total number of consultations).

The frequency of the different POC-US examinations will be summarized in relation to the organs scanned (Q13). The performed POC-US examinations are defined as ***organs scanned*** and not as standardized procedures such as FAST, FATE or LUS since there might be differences in the definition and interpretation of these examinations. The ***organs scanned*** are registered on a list of organs in the questionnaire. The GPs can choose to write in free text if organs are missing from the list.

5.1.3 Time consumption:

The GPs will measure the time used for the POC-US examination. This time registration (Q12) will be described in minutes for each type of POC-US examination (Q13).

5.1.4 Modification:

By the before and after registration of the organs intended to scan (Q 7) and the organ actually scanned (Q13), the extent of modification of POC-US to include e.g. opportunistic screening, can be estimated. The modification of the performed POC-US will be described in frequencies of POC-US examinations that are reduced, expanded or unchanged.

How often are the GPs able to produce POC-US pictures of relevant structures (Q14) will be summarized for all organs scanned and described in overall frequencies.

5.1.5 Findings:

The findings in POC-US are measured through the categorial variables *certain positive findings, uncertain positive findings, certain negative findings, uncertain negative findings, and incidental findings* (Q 15). The findings will be described in frequencies and we will also describe the relationship between certain findings and change in treatment and plan for the patient.

5.2 How POC-US influences the diagnostic process:

5.2.1 Change in diagnose:

The GPs are asked to declare the tentative diagnoses as one main tentative diagnosis (Q8) and other possible diagnoses (Q9.1) before the use of POC-US. After the use of POC-US the GPs will be shown

their “Before-US” tentative diagnoses (Q8 and Q9.1) and asked if these diagnoses have changed (Q16). If the diagnoses have changed, they will be asked to specify this (Q16.1 and Q16.2.1).

The tentative diagnoses are registered as ICPC2 codes in the questionnaire. Change in the tentative diagnoses is measured in the frequency of GPs’ declaration of change and in overall registered change in the ICPC2 codes.

5.2.2 Change in confidence:

The GPs are asked to register any change in their confidence in the tentative diagnoses after the use of POC-US (Q 17) by choosing one of the following variables on an ordinal scale: *Increased confidence, more confident, unchanged confidence, less confident, reduced confidence*.

To test the reliability of the GPs’ declaration of confidence (Q 17), we will examine if an increased confidence is correlated to specific organs scanned (Q 13), a reduction in the total number of diagnoses (NBD and NAD), or a change from symptom diagnosis to disease diagnosis (Q8 and Q16.1).

5.3 How POC-US affects the treatment of the patients:

5.3.1 Change in the plan for the patient

The GPs register their plan for the patient by choosing one or more of the following categorical variables before (Q10) using POC-US: *Acute admission to hospital, subacute referral to hospital, normal referral to hospital, subacute referral to specialist, normal referral to specialist, referral for radiology, other referral e.g. to physiotherapist, follow-up in the clinic, no plan for follow-up, other*.

After using POC-US the GP is shown the “before POC-US plan for the patient” and asked if this plan has changed (Q18). If the plan has changed, the GP is asked to specify (Q18.1).

Change in the plan for the patient is defined as the frequency of declared change and elaborated on in this before and after registration from one possible answer to another, or change in the number of possible answers.

5.3.2 Change in the treatment for the patient

The GPs register their initiated treatment before POC-US (Q11) by choosing one or more of the following categorical variables: *Referral for treatment in the secondary sector, medication, other treatment, no treatment, other*. After using POC-US the GP is shown the “before POC-US planned treatment for the patient” and asked if this planned treatment has changed (Q19). If the planned treatment has changed, the GP is asked to specify (Q19.1)

Change in the initiated treatment of patients is defined as the frequency of declared change and elaborated on in this before and after registration from one possible answer to another, or in the number of possible answers.

6 Study Methods

6.1 General Study Design and Plan

This is a prospective observational cohort study. The participating GPs fill out questionnaires before and after using POC-US.

6.2 Study Variables

Question Q1-Q11 are presented before POC-US, while Q12-Q19.1 are presented after POC-US.

Between Q11 and Q12 there is a time-log with three variables:

6.2.1 Questions BEFORE the use of POC-US:

Question number	Question	Possible answers	Validation rule
Q 1	GP ID	A to T	Only two number
Q 2	Patient ID	A1 to T200	Only 1-3 numbers
Q 3	Date	2018-01-15 to 2018-08-15	YYYY-MM-DD
Q 4	Patient gender	1. Male 2. Female	Single-choice
Q 5	Patient Age	0-120	Only 1-3 numbers
Q 6	What is the main reason to use POC-US in this patient?	1. Rule-in/Rule-out 2. Explore	Single-choice
Q 7	Which organs/positions do you expect to scan?	Heart, lungs, cheat, thyroid, lymph nodes, skin, gall bladder, liver, kidney, pancreas, ascites, bladder, uterus, ovaries, placenta, fetus, fluid in fossa douglasi, aorta, veins, carotid, blood vessels, joints, muscles, tendons, bone, other.	Multiple-choice
Q 8	What is the main tentative diagnosis for this patient?	Type a ICPC2 code	Letter followed by 2 numbers
Q 9	Are there any other possible tentative diagnoses in this case?	1 Yes*	Single-choice

		2 No	
*Q 9.1	Which other diagnoses do you have for this patient?	Type in a “2. ICPC2 code” “3. ICPC2 code” “4. ICPC2 code”	Letter followed by 2 numbers 1 must be answered, 2-4 are optional
Q 10	What is your overall plan for this patient?	1 Acute admission to hospital 2 Subacute referral to hospital 3. Elective referral hospital 4. Subacute referral to specialist 5. Elective referral to specialist 6. Referral to radiology 7. Other referral e.g. physiotherapist 8. Follow-up in the clinic 9. No plan for follow-up 10. Other, please declare	Multiple-choice 10. must be elaborated in textbox
Q 11	Which treatment will you initiate at this stage?	1. Medication 2. I will refer for treatment 3. I will initiate other treatment 4. None 5. Other, please declare	Multiple-choice 5. must be elaborated in textbox

6.2.2 Questions AFTER the use of POC-US:

Question	Question	Possible answers	Validation rule
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number			
Q 12	How much time did you use on the POC-US examination?	Type number of Minutes (1-999)	1-3 numbers
Q 13	Which organs/positions did you scan?	Heart, lungs, cheat, thyroid, lymph nodes, skin, gall bladder, liver, kidney, pancreas, ascites, bladder, uterus, ovaries, placenta, fetus, fluid in fossa douglasi, aorta, veins, carotid, blood vessels, joints, muscles, tendons, bone, other.	Multiple-choice
Q 14	<p>Were you able to produce ultrasound images of the relevant structures of (inserted text) ?</p> <p><i>This questions is repeated for each organ chosen in Q7 and Q13, with the organs as the inserted text</i></p>	<p>1. Yes</p> <p>2. No – why not?</p>	<p>Single-choice</p> <p>2. must be elaborated in textbox</p>
Q 15	What did you find?	<p>1. Certain positive findings</p> <p>2. Uncertain positive findings</p> <p>3. Certain negative findings</p> <p>4. Uncertain negative findings</p> <p>5. Incidental findings – please declare</p>	<p>Multiple-choice</p> <p>5.must be elaborated in textbox</p>
Q 16	<p>Before POC-US you registered these tentative diagnoses (inserted text)</p> <p>Have your tentative diagnoses changed?</p> <p><i>The inserted text is ICPC2 codes from Q8 and Q9.1</i></p>	<p>1. Yes, the diagnoses have changed but the ICPC2 codes are the same</p> <p>2. Yes, the diagnoses have changed and the ICPC2 codes have also changed*</p> <p>3.No</p>	Single-choice
*Q 16.1	What is the main tentative diagnosis	Type ICPC2 code	Letter followed

	for this patient now?		by 2 numbers
*Q 16.2	Do you have any other possible tentative diagnoses for this patient (please specify)?	1 Yes** 2. No	Single-choice
**Q 16.2.1	Which other diagnoses do you have for this patient?	Type in a “2. ICPC2 code” “3. ICPC2 code” “4. ICPC2 code”	Letter followed by 2 numbers 1 must be answered, 2-4 are optional
Q 17	How is your confidence in your main tentative diagnosis, after you have used POC-US?	1. Highly increased confidence 2. More confidence 3. unchanged confidence 4. Less confidence 5. Highly reduced confidence.	Single-choice
Q 18	Before POC-US you registered this plan (inserted text) for the patient. Has your overall plan changed? <i>The inserted text is the plan chosen in Q10</i>	Yes* No	Single-choice
*Q 18.1	What is your overall plan for this patient, now?	1 Acute admission to hospital 2 Subacute referral to hospital 3. Elective referral hospital 4. Subacute referral to specialist 5. Elective referral to specialist 6. Referral to radiology 7. Other referral e.g.	Multiple-choice 10. must be elaborated in textbox

		physiotherapist 8. Follow-up in the clinic 9. No plan for follow-up 10. Other, please declare	
Q 19	Before POC-US you registered this treatment (inserted text) for the patient. Has your initiated treatment for this patient changed? <i>The inserted text is the treatment chosen in Q11</i>	Yes* No	
*Q 19.1	Which treatment will you initiate at this stage?	1. Medication 2. I will refer for treatment 3. I will initiate other treatment 4. None 5. Other, please declare	Multiple-choice 5. must be elaborated in textbox

*The Questions marked with * are activated questions. When * appears after the answer-category, it means that this answer activates a new questions, marked with a * before the question-number. Activated questions (marked with *) have question-numbers that states the connection.*

6.3 Other collected variables:

Time-log (T1-T3):

We will have a java script on a page between the "before" and the "after" questions, this java script will create the following variables:

- T1: The exact time when Q11 is finished
- T2: The exact time when Q12 begins
- T3: calculated time in seconds between T1 and T2

Number of excluded patients during the study period for each GP

The included GPs will register the number of excluded patients during the study period together with reason for exclusion.

Number of consultations (NC) for each GP:

The included GPs will provide information on the total number of face-to-face consultations they have during the study period, not including planned preventive consultations or home visits. This variable is labeled *number of consultations* (NC) and will be different for each included GP.

Background information on the GPs: see section 9.1

6.4 Calculated variables:

Frequency of POC-US for each GP (FUS)

Calculating the proportion of patients with a POC-US examination during the study period (summarizing included and excluded patients) out of the total number of consultations for each GP (NC)

Modification of POC-US

Any modification of the POC-US examination is calculated as the difference between organs intended to scan (Q 7) and organs scanned (Q 13) and described in frequencies of POC-US examinations that are reduced, expanded or unchanged.

Number of possible tentative diagnoses before POC-US (NBD)

Summarizing the number of declared ICPC2 codes in Q8 and Q9.1

Number of possible tentative diagnoses after POC-US (NAD)

Summarizing the number of ICPC2 codes in Q16.1 and Q16.2.1

Change in the ICPC-2 code of the main tentative diagnosis after US (CMD)

Calculating the frequency of change between the before (Q8) and after (Q 16.1) registration of the main tentative diagnosis

Change in the total number of tentative diagnoses (CND)

Calculating the frequency of change in the total number of tentative diagnoses (NBD and NAD)

Change from symptom to disease diagnoses (CSD)

Calculating the frequency of change from symptom diagnosis (ICPC 2 1-29) in the main diagnosis before POC-US (Q 8) to disease diagnosis (ICPC 2 70-99) in the main diagnosis after POC-US (Q16.1)

Change in the number of plans for the patient (CNP)

Calculating the frequency of change in the number of possible answers chosen in the before (Q10) and after (Q18.1) plan for the patient.

Change in the number of treatments for the patient (CNP)

Calculating the frequency of change in the number of possible answers chosen in the before (Q11) and after (Q19.1) treatment for the patient.

7 Sample Size

The overall aim of this study is to describe how POC-US is used in Danish general practice. Based on a pilot questionnaire (unpublished data) and an interview study (not yet published), we estimate that there are around 75 GPs in Denmark, who use POC-US. We find it realistic to include 20 GPs in this study. This sample size will enable us to have some variation (geographical, experience, etc) among the included GPs.

We estimate from our own experience and from talks with GPs, who scan, that the GPs will use POC-US 2-3 times a day, and assuming a participation rate of 80%, we will therefore have 640-960 US scan during the study period of one month. This number of scans is expected to be sufficient to give a valid statistical description of e.g. frequencies of organs scanned and other outcomes. Additionally, it is a sufficiently large number of scans to enable an evaluation of safety when we later on make the six months follow-up. We hope to maintain the GPs' dedication to the project by the relative short study period (one month).

8 General Considerations

8.1 Timing of Analyses

The analyses will begin after all included GPs have completed their data collection and all collected data, including any paper versions of the questionnaire, have been received at RUGP-Aalborg.

If there is multiple registrations on the same patient-ID, we will contact the GP and ask for elaboration. Only one registration per patient-ID will be included for further analysis.

8.2 Missing Data

Missing data are coded as "." and we will report the number of missing values for each variable.

The questionnaire in SurveyXact is designed with validation rules to avoid missing values. However, a GP may abort the questionnaire leaving questions unanswered.

If the time-log register T3 to be less than 1 minute and the GP registers a duration of the POC-US > 1 minute (Q12), we will assume, that there was no "before and after" registration, but only an "after" registration. In that case, we will exclude the "before" answers (Q1-Q11). In paper-version of the questionnaire, the GPs will be asked to provide a registration of the exact time after finishing question 11 and before starting question 12. If the difference between the two registrations is less than 1 minute and the GP registers a duration of the POC-US > 1 minute (Q12), we will assume, that there was no "before and after" registration, but only an "after" registration.

9 Summary of Study Data

We will use descriptive statistics. The questionnaire will mainly collect data on nominal scales. However, *Confidence after POC-US* (Q17) will be measured on an ordinal scale and *Time consumption* (Q12) and *patient age* (Q5), on a ratio scale.

The calculated variables (*Frequency of POC-US for each GP (FUS)*, *Modification of POC-US*, *Number of possible tentative diagnoses before POC-US (NBD)*, *Number of possible tentative diagnoses after POC-US (NAD)*, *Change in the ICPC-2 code of the main tentative diagnosis after US (CMD)*, *Change in the total number of tentative diagnoses (CND)*, *Change from symptom to disease diagnoses (CSD)*, *Change in the number of plans for the patient (CNP)*, and *Change in the number of treatments for the patient (CNP)*) will be described in frequencies.

The categorical variables will be described using absolute frequencies tables and chi-square or Fishers exact test to test if the differences in the observed frequencies are statistically significant. We will consider a p-value of 0.05 statistical significant.

If the continuous variables are normally distributed, they will be reported with means and either a standard deviation or a 95% confidence interval of the mean; if not normally distributed, with a median and interquartile range.

10 Demographic and Baseline Variables

As part of the recruitment process for this study, interested GPs will answer a questionnaire containing the following background characteristics:

10.1 Baseline questions to describe the participating GPs (BQ):

Question number	Question	Catagory
BQ 1.1	How old are you?	Age
BQ 1.2	Are you a woman/man?	Gender
BQ 1.3	How many years have you been a GP?	Experience
BQ 1.4	Which year did you graduate as a doctor?	Experience
BQ 1.5	How long have you been using ultrasound?	Experience
BQ 1.6	Would you characterize your practice as predominantly rural, urban or mixed	Location
BQ 1.7	How is your practice organized? (solo, partnership, collaboration)	Organization
BQ 1.8	How many patients are assigned to your practice?	Organization
BQ 1.9	How many days a week do you do clinical work?	Organization
BQ 2.0	In which region do you practice?	Location
BQ 2.1	What is the approximate distance in kilometers from your practice to the nearest radiology department where US can be performed?	Location
BQ 2.2	What kind of US device (name, model, year) and probes do you have?	Equipment
BQ 2.3	What kind of ultrasound education/training did you receive?	Experience
BQ 2.4	Which anatomical areas do you scan with ultrasound?	Use
BQ 2.5	How often do you use ultrasound?	Frequency
BQ 2.6	Do you have a conflict of interest, participating in this study?	COI

10.2 Base-line assessment of GPs

We will evaluate the GPs' technical skills at baseline. After inclusion, each participating GP will be asked to perform POC-US in a standardized setting and reviewed by an external reviewer (radiologist) using the standardized protocol, providing a score for each participant (OSAUS).

11 Reporting Conventions

P-values ≥ 0.001 will be reported to 3 decimal places; p-values less than 0.001 will be reported as “<0.001”. Frequencies and other statistics will be reported with to one decimal.

12 Technical Details

Data will be collected through the web-based analysis tool SurveyXact, provided by Rambøll Management through Aalborg University, Denmark. Data will be exported from SurveyXact in an excel-file. The file is saved on a secure server at Aalborg University in an allocated drive, and can only be assessed by the research team through passwords.

Analysis will be conducted using STATA version 14 (StataCorp, Texas, USA) by the principal investigator Camilla Aakjær Andersen. Martin Bach Jensen will review the results and log-files.

13 Additions

13.1 First addition to the original SAP

After datacollection had completed it was decided to include subanalysis for the individual participants in order to describe:

- The frequencies of participating GPs (Q1), who performed focused/explorative POC-US examinations (Q6)
- The frequency of participating GPs (Q1), who performed POC-US examinations with certain organs (Q13)
- The frequency of participating GPs (Q1), who performed POC-US examinations (Q13) in line with their pervious training (BQ 2.3)
- The frequency of participating GPs (Q1), who performed POC-US examinations (Q13) in line with their predefined curriculum (BQ 2.4)
- The frequency of participating GPs (Q1), who performed POC-US examinations that they were skilled to perform (OSAUS).